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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/046,433 | 01/16/2002 | Jian Ni | PF511P1 | 3443 |

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| EXAMINER |
|---|
| O'HARA, EILEEN B |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | 5 |

DATE MAILED: 01/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/046,433 | NI ET AL. | |
| | Examiner | Art Unit | |
| | Eileen B. O'Hara | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 63 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-63 are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

A. Claims 1-33, drawn to polynucleotides, vectors, host cells and recombinant method of producing protein, classified in class 536, subclass 23.5, class 435, subclasses 320.1, 252.3 and 69.1, for example.

B. Claims 40-43, drawn to polypeptides, classified in class 530, subclass 350, for example.

C. Claims 44 and 45, in so far as they are drawn to antibodies, classified in class 530, subclass 388.22, for example.

D. Claims 46, 47, 52, 53, 59, 60 and 63, in so far as they are drawn to a method of treatment comprising administering a polypeptide of Group II, classified in class 514, subclass 2, for example.

E. Claims 46-63, drawn to a method of treatment comprising administering an agonist to the polypeptide of Group B, classified in class 514, subclass 2, for example.

F. Claims 46-63, drawn to a method of treatment comprising administering an antagonist to the polypeptide of Group B, classified in class 514, subclass 2, for example.

G. Claims 74 and 87-92, in so far as they are drawn to gene therapy, classified in class 514, subclass 44.

Applicant is advised that claims 1, 31-33 are improper Markush claims because the nucleic acids recited there do not serve common functions which are based upon a common property or special technical feature not found in the prior art. The polynucleotides of TR13 and TR14 are distinct and separate inventions because they have different nucleic acid sequences and encode distinct proteins that have different amino acid sequences, structures and functions. In addition, the nucleic acids recited in claims 31-33, SEQ ID NOS: 8-22 and 48-59 are disclosed on page 21 of the specification only as having nucleotide sequences related to extensive portion of TR13 or TR14, and therefore appear not to be parts of those inventions. Additionally, because the nucleic acids and proteins of TR13 and TR14 are unrelated, antibodies, agonists and antagonists to TR13, and methods of using the polynucleotides, polypeptides, antibodies, agonists and antagonists of TR13, are unrelated to antibodies, agonists and antagonists to TR14, and methods of using the polynucleotides, polypeptides, antibodies, agonists and antagonists of TR14.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions A and B are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or

(2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polynucleotide is related to the polypeptide by virtue of encoding the same. The polynucleotides have utility for the recombinant production of protein in a host cell. Although the polynucleotides and proteins are related since the polynucleotides encode the specifically claimed proteins, they are distinct inventions because the protein products can be made by another materially different process, such as by synthesis or purification from the natural source. Further, the polynucleotides may be used for processes other than the production of proteins, such as nucleic acid hybridization assays and gene therapy.

The proteins of invention B are related to the antibodies of invention C by virtue of being the cognate antigen, necessary for the production of the antibodies. Although the protein and antibody are related due to the necessary stearic complementarity of the two, they are distinct inventions because they are physically and functionally distinct chemical entities, and because the protein can be used in another and materially different process from the use for production of the antibody, such as in a pharmaceutical composition in its own right, or to assay or purify the protein.

Invention A is related to Invention G as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotides can be used in a method gene therapy of invention F, but the polynucleotides may also be used in a method of detecting the presence of a nucleic acid molecule in a sample by hybridization, both of which are materially different methods that have different starting compounds, method steps and goals.

Inventions B and D are related as product and process of use. In the instant case, the polypeptides can be used in a method of treatment, but the polypeptides may also be used in a method of making antibodies, which is a materially different method.

Invention C is related to each of inventions E and F as product and process of use. In the instant case, the antibodies to the polypeptides may be agonists or antagonists of the polypeptides and can be used in a method of treatment, but the antibodies may also be used in a method of purifying the polypeptides, which is a materially different method.

Inventions A and each of inventions C, D, E and F are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the polynucleotides and antibodies are distinct inventions because they are structurally and functionally distinct chemical compounds, and the polynucleotides are not used in the methods of inventions D, E and F.

Invention B and each of inventions E, F and G are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the polypeptides are not used in the methods of inventions E, F and G.

Invention C is unrelated to each of inventions D and G. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the antibodies to the polypeptides are not used in the methods of inventions D and G.

Inventions D-G are also not related to each other. The methods of the different inventions require different starting compounds and have different steps and goals.

3. ***Further Restriction Within Groups A-G***

***Further Restriction within Groups A or G***

Applicants' claims are drawn to numerous patentably distinct nucleic acid sequences or methods of gene therapy using the nucleic acids. If group A or G is elected, further restriction *within* the groups is required, as follows:

The claims are drawn to numerous patentably distinct nucleic acids, each of which constitutes a patentably distinct product. Applicant is required to elect a single invention of a nucleic acid, selected from the group consisting of: (i.e. elect one from the following Markush group): a nucleic acid comprising a polynucleotide selected from the group consisting of the following, TR13 nucleic acid of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO: 2, TR13 nucleic acid of SEQ ID NO: 39 encoding a polypeptide of SEQ ID NO: 40, TR14 nucleic acid of SEQ ID NO: 4 encoding a a polypeptide of SEQ ID NO: 5, TR14 nucleic acid of SEQ ID NO: 60 encoding a a polypeptide of SEQ ID NO: 61, nucleic acid of SEQ ID NO: 8, nucleic acid of SEQ ID NO: 9, nucleic acid of SEQ ID NO: 10, nucleic acid of SEQ ID NO: 11, nucleic acid of SEQ ID NO: 12, nucleic acid of SEQ ID NO: 13, nucleic acid of SEQ ID NO: 14, nucleic acid of SEQ ID NO: 15, nucleic acid of SEQ ID NO: 16, nucleic acid of SEQ ID NO: 17, nucleic acid of SEQ ID NO: 18, nucleic acid of SEQ ID NO: 19, nucleic acid of SEQ ID NO: 20, nucleic acid of SEQ ID NO: 21, nucleic acid of SEQ ID NO: 22, nucleic acid of SEQ ID NO: 48, nucleic acid of SEQ ID NO: 49, nucleic acid of SEQ ID NO: 50, nucleic acid of SEQ ID NO: 51, nucleic

acid of SEQ ID NO: 52, nucleic acid of SEQ ID NO: 53, nucleic acid of SEQ ID NO: 54, nucleic acid of SEQ ID NO: 55, nucleic acid of SEQ ID NO: 56, nucleic acid of SEQ ID NO: 57 or nucleic acid of SEQ ID NO: 58.

***Further Restriction within Groups B-G***

Applicants' claims are drawn to numerous patentably distinct polypeptide sequences, antibodies to, and methods of treating using polypeptides or agonists or antagonists of the polypeptides. If one of groups B-F is elected, further restriction *within* the groups is required, as follows:

The claims are drawn to numerous patentably distinct polypeptides and antibodies to (including both agonists and antagonists), each of which constitutes a patentably distinct product. Applicant is required to elect a single invention of a polypeptide or antibody to selected from the group consisting of: (i.e. elect one from the following Markush group): a TR13 polypeptide of SEQ ID NO: 2, a TR13 polypeptide of SEQ ID NO: 40, a TR14 polypeptide of SEQ ID NO: 5, and a TR14 polypeptide of SEQ ID NO: 61.

To be fully responsive to this requirement, Applicants are **required** to point out which claims correspond to the elected invention. Applicant is advised that this is not a species election.

Although the classifications for these various nucleic acids are overlapping, for instance 536/23.1 or 530/350, each represents a patentably distinct product with distinct physical and

functional characteristics. For example, even though SEQ ID NOS: 5 and 61 are identified as TR14 polypeptides, there is significant divergence at the N-terminus. The two sequences are 45% different in the extracellular domain, and would require separate sequence searches and consideration. Additionally, the nucleic acid sequences of SEQ ID NOS: 8-22 and 48-59 are identified as being related to regions of either TR13 or TR14 nucleic acid sequences, and are therefore different sequences that would require separate searches. The search for more than one product would be burdensome, because, in the case of the nucleic acid sequences, many are claimed not by nucleic acid sequence, but by the sequence of the protein encoded thereby, and requires a search of the corresponding region of SEQ ID NO: 1 as well as a 'reverse translation' search of the corresponding region of SEQ ID NO: 2, such that each individual sequence requires two sequence searches which are not required for any of the other sequences, or alternatively by virtue of comprising only a small portion of a disclosed nucleic acid or polypeptide, which requires a separate "word search" of the nucleic acid and protein databases. Due to the use of 'comprising' language, it cannot even be said that the search for nucleic acids encoding amino acids 1-226 of SEQ ID NO:5 would reveal art pertaining to, for instance a nucleic acid *comprising* a region encoding amino acids 42-52 of SEQ ID NO: 5, as the latter could be found embedded in a completely different protein. Additionally, the logarithmic growth of the sequence databases makes searching for more than one product burdensome. Accordingly, restriction is proper.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art either because of their different classification, recognized divergent

subject matter, and/or the need for non-coextensive literature search, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(i).

***Advisory Information***

Applicant is advised that SEQ ID NO: 1 is identified in claim 1(b)-(c) as a polypeptide, but it is a nucleotide sequence.

Applicant is further advised that claim 7 identifies SEQ ID NO: 39 and 40 as being TR14, but the specification on page 4 identifies the sequences as being TR13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER